



Perioperative and Oncological Outcomes of Partial Versus Radical Nephrectomy for Complex Renal Tumors (RENAL Score ≥ 7): Systematic Review and Meta-Analysis

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ABSTRACT

Objective. Which is superior, partial nephrectomy (PN) or radical nephrectomy (RN), for the treatment of complex renal tumours (RENAL or score ≥ 7)?

Methods. This systematic review and meta-analysis was conducted in accordance with the PRISMA statement. A systematic search of the literature published before November 2023 was conducted using Pubmed, Embase, Cochran, and Web of Science libraries. We included studies comparing perioperative and oncologic outcomes of partial nephrectomy and radical nephrectomy for complex renal tumors.

Results. A total of 2602 patients from six studies meeting the criteria were included. The PN group had a longer operative time, increased estimated blood loss, and major complications but a smaller reduction in renal function. There were no significant differences in complications, length of hospital stay, and blood transfusion. In terms of oncological outcomes, the PN group had longer OS, CSS, and no significant difference in RFS.

Conclusions. For complex renal tumours, PN requires more operative time and has a higher chance of complications in the short term. However, in long-term follow-up, PN has a small decrease in renal function with longer OS and CSS.

Keywords Partial nephrectomy (PN) · Radical nephrectomy (RN) · Complex renal tumours · Meta-analysis

The incidence of renal cell carcinoma accounts for 3% to 5% of malignant tumours in adults and is second only to prostate and bladder cancers among male urological malignancies.¹ The incidence of renal cell carcinoma increases every year in most regions.² Surgery is the treatment of choice for limited renal cell carcinoma, and the current surgical approach, for limited renal cell carcinoma are partial nephrectomy (PN) and radical nephrectomy (RN).³ To predict the complexity of PN and the possibility of complications, surgeons use RENAL, PADUA, and C-index nephrometry scoring systems, as well as other renal measurement scoring systems to quantify the possibility of related renal tumors and complications.⁴ The Renal Tumour Surgery Scoring System is based on the deconvolutional characteristics of renal tumours and consists of Radius (tumor size as maximal diameter), Exophytic/endophytic properties of the tumor, Nearness of tumor deepest portion to the collecting system or sinus, Anterior/posterior descriptor, and the Location relative to the polar line.^{5,6} It is now generally accepted that PN better preserves renal function, reduces the risk of renal insufficiency and associated cardiovascular events, and has an OS benefit in some populations.^{7–9} Partial nephrectomy is indicated for patients with renal tumours at stage T1, located on the surface of the kidney, and amenable to surgical manipulation.¹⁰ However, the efficacy of PN for the treatment of complex renal masses (RENAL score ≥ 7) remains controversial. Although several recent studies have compared the perioperative and oncological outcomes of PN

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and RN for the treatment of complex renal tumours, most of them have been limited to a single medical centre.

Therefore, we conducted a systematic review and meta-analysis of articles using the RENAL score to assess perioperative and oncological outcomes and to assess whether anatomical complexity of renal tumours affects perioperative and oncological outcomes.

METHODS

Literature Search

We performed a systematic review and cumulative meta-analysis of the primary outcomes of interest according to the PRISMA criteria, following AMSTAR guidelines for quality assessment.¹¹ This systematic review has been registered with PROSPERO.

The literature search and screening process is carried out independently by two researchers, and if there is a disagreement and no agreement can be reached, a third examiner participates in the decision. Four databases were searched: Embase, PubMed, Cochrane Library, and Web of Science. The search period was from the creation of each database to November 2023. Search terms included: ("complex renal tumours" or complex) and ("partial nephrectomy" or PN) and ("radical nephrectomy" or RN), and synonyms of these terms. Hand-searching reference lists of relevant studies broadened the scope of the search.

Eligibility Criteria

Reports were included in our systematic review if they met the inclusion criteria: (1) study subject diagnosed with renal carcinoma and undergoing PN or RN; (2) comparison was made according to RENAL score; and (3) contain at least one outcome, including operation time (OT), length of stay (LOS), estimated blood loss (EBL), complications, overall survival (OS), cancer-specific survival (CSS), relapse-free survival (RFS). Exclusion criteria included: (1) inability to extract applicable data; (2) research in the form of editorials, meetings, expert opinions; (3) the overlapping study population reported the same results; (4) the study subject is nonhuman; and (5) not grouped according to surgical approach.

Data Extraction

Two independent reviewers independently selected articles for inclusion and extracted the data according to a pre-established data collection form. Extracted data included: author, year of publication, sample size, age, document type, surgical approach, operative time, length of hospital stay,

estimated blood loss, complications, transfusions, OS, CSS and RFS.

Study Quality Assessment

Retrospective studies were assessed using the Newcastle-Ottawa (NOS) scale.¹² The NOS scores range from 0 to 9; more than 6 was considered high quality.

Risk of Bias Assessment

The risk of bias assessment in the included studies was conducted by the same two authors independently. The ROBINS-I tool was used to assess the risk of bias in non-randomized studies. The ROBINS-I tool includes seven domains: confounding bias, selection bias, intervention measurement classification bias, bias due to deviations from the intended intervention, bias due to missing data, outcome measurement bias, and reported outcome selection bias.¹³ Because fewer than ten studies were included, we did not perform a risk of bias assessment.

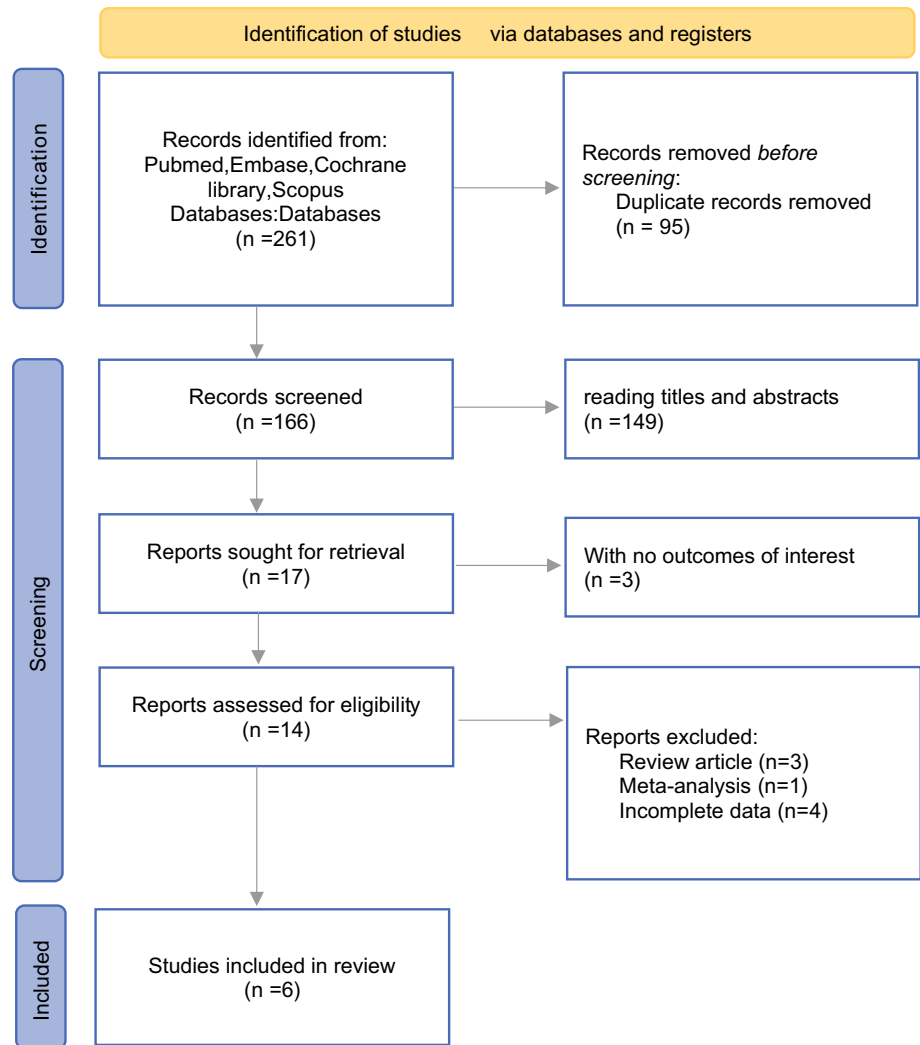
Data Analysis

We used Stata version 16.0 tool for data analysis. We use log RR (relative risk), SMD, and the variance as the summary outcome measure from all trials in the meta-analysis. For each trial, HR (hazard ratio) with the 95% confidence intervals (CI) of the survival rate was derived and calculated using either the fixed effects model or the random-effects model.¹⁴ Statistical significance was defined as $P < 0.05$. Chi-square and q-test were used to verify the heterogeneity among the included studies, such as $I^2 > 50\%$ or $P < 0.10$, indicating significant heterogeneity between studies, and a random-effects model was selected.

RESULTS

Description of Study

The authors searched 251 records from four databases and manually searched ten records from the reference lists of relevant studies. Ninety-five duplicate articles were eliminated using document management software; 149 articles were excluded from reading titles and abstracts; 17 studies were included in careful reading, excluding three studies with no outcomes of interest, three systematic reviews, one meta-analysis, and four incomplete data. A total of 261 studies were included, and six studies were finally included for meta-analysis.^{15–20} The screening process is shown in Fig. 1, and the baseline characteristics of the included studies are shown in Table 1. Six publications were published from 2016 to 2023, including 2602 patients. In addition,

FIG. 1 Selection process**TABLE 1** Baseline data for studies included in the meta-analysis

Study	Year	Type	Sample (n)	Age (years)	BMI (kg/m ²)	Tumor size (cm)	Center	Operation
Cerrato C.	2023	Retrospective	921	60	28.9	7.5	Single Center	MIS-RN ^b RALPN ^c
Cerrato C.	2023	Retrospective	969	60.6	28.2	6.5	Single Center	MIS-RN RALPN
Zhang X.	2021	Retrospective	314	58.2	27.4	NA	Single Center	OPEN Laparoscopic
Long G.	2020	Retrospective	132	55.4	24.9	8.1	Single Center	OPEN Laparoscopic
Deng W.	2020	Retrospective	148	48.7	NA	6.4	Single Cente	LRN ^b LPN ^d
Liu T. Y.	2016	Retrospective	118	43.3	43.4	6.3	Single Cente	OPEN Laparoscopic

BMI body mass index; *MIS-RN* minimally invasive radical nephrectomy; *LRN* laparoscopic radical nephrectomy; *RALPN* robot-assisted laparoscopic partial nephrectomy; *LPN* laparoscopic partial nephrectomy

the sample size was 118–969. Six of the studies were retrospective.

Quality Assessment

The quality of the cohort studies was evaluated by using the modified Newcastle-Ottawa Scale, NOS score was 6 to 8 points in Table 2.²¹ Six studies of high quality were included, all with a score of 6 or more in Table 2.

Operation Time

Four studies reported OT. Because of high heterogeneity ($I^2 = 89.4\%$, $P = 0.000$), we used a random-effects model. The pooled meta-analysis demonstrated significant difference

between RN and PN (SMD = -0.59 , 95% CI $[-1.14, -0.04]$, $P < 0.05$; Fig. 2).

Length of Stay

Four studies reported LOS. Because of high heterogeneity ($I^2 = 98.2\%$, $P = 0.000$), we used a random-effects model. The pooled meta-analysis demonstrated no significant difference between RN and PN (SMD = -0.61 , 95% CI $[-1.60, 0.39]$, $P > 0.05$; Fig. 3).

Estimated Blood Loss

Three studies reported EBL. Because of high heterogeneity ($I^2 = 73.1\%$, $P = 0.024$), we used a random-effects model. The pooled meta-analysis demonstrated significant

TABLE 2. Quality score of included studies based on the NOS scale

Study	Selection			Comparability			Exposure			Total stars
	REC	SNEC	AE	DO	SC	AF	AO	FU	AFU	
Cerrato C.	1	1	1	1	1	1	1			7
Cerrato C.	1	1	1	1	1		1	1		7
Zhang X.	1	1	1	1	1		1		1	7
Long G.	1	1	1	1	1		1	1		7
Deng W.	1	1	1	1	1	1	1			7
Liu T. Y.	1	1	1	1	1		1	0		6

REC representiveness of the cohort; SNEC selection of the none posed cohort; AE ascertainment of exposure; DO demonstration that outcome of interest was not present at start of study; SC study controls most important factors; AF study controls for other important factors; AO assessment of outcome; FU follow-up long enough for outcomes to occur; AFU adequacy of follow-up of cohort ($\geq 80\%$)

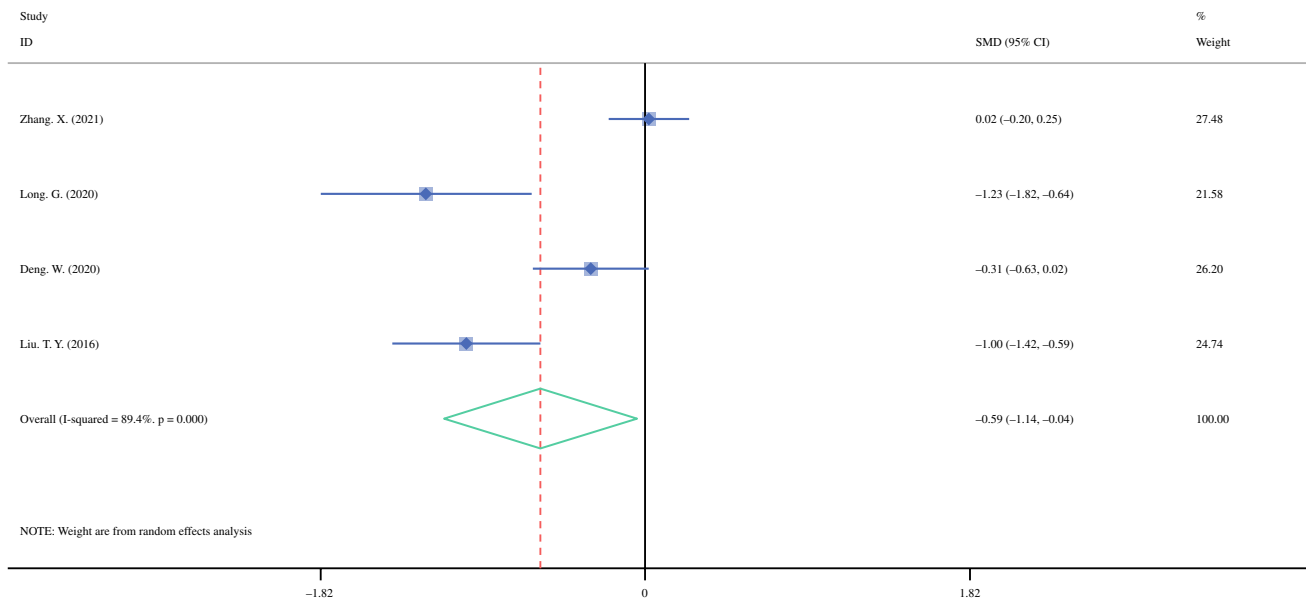


FIG. 2 Forest plot and meta-analysis of OT between RN and PN scores

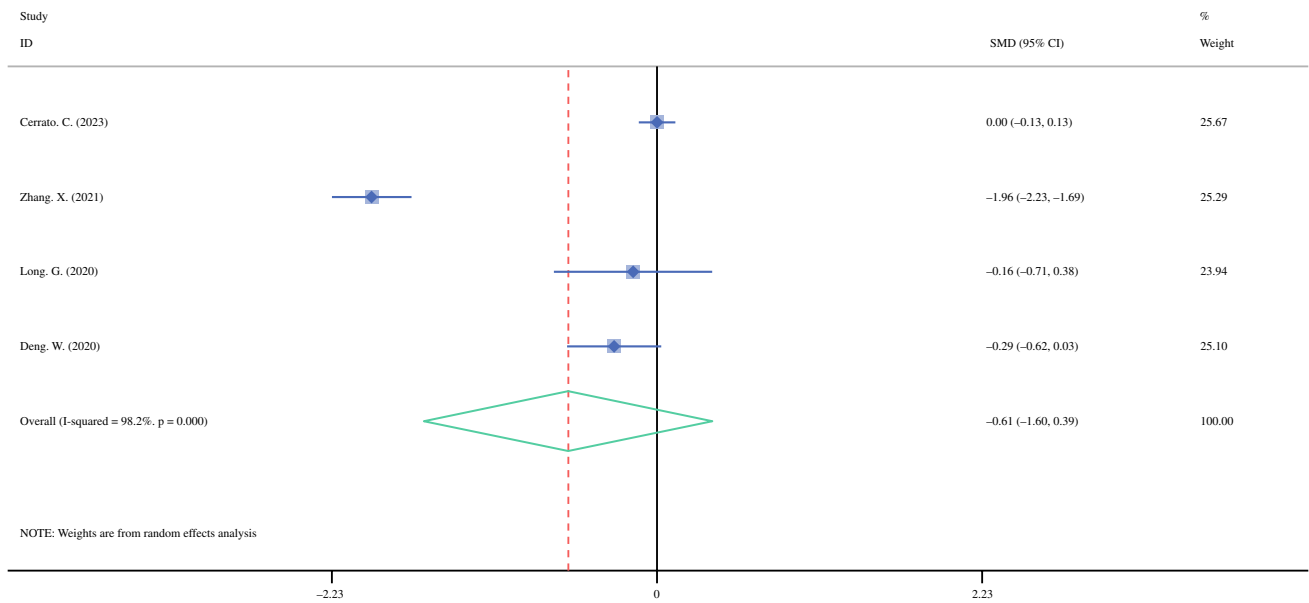


FIG. 3 Forest plot and meta-analysis of LOS between RN and PN scores

difference between the RN and PN (SMD = -0.51, 95% CI [-0.90, -0.12], $P < 0.05$) (Fig. 4).

Complications

Four studies reported complications. Because of high heterogeneity ($I^2 = 80.7%$, $P = 0.001$), we used a random-effects model. The pooled meta-analysis demonstrated no significant difference between the RN and PN (RR = 0.72, 95% CI [0.34, 1.50], $P > 0.05$) (Fig. 5).

Four studies reported major complications (Clavien-Dindo score ≥ 3). Because of low heterogeneity ($I^2 = 0.0%$, $P = 0.728$), we used a fixed-effects model. The pooled meta-analysis demonstrated significant difference between the RN and PN (RR = 0.46, 95% CI [0.26, 0.80], $P < 0.05$) (Fig. 6).

Blood Transfusion Needs

Four studies reported blood transfusion needs. Because of low heterogeneity ($I^2 = 13.8%$, $P = 0.323$), we used a

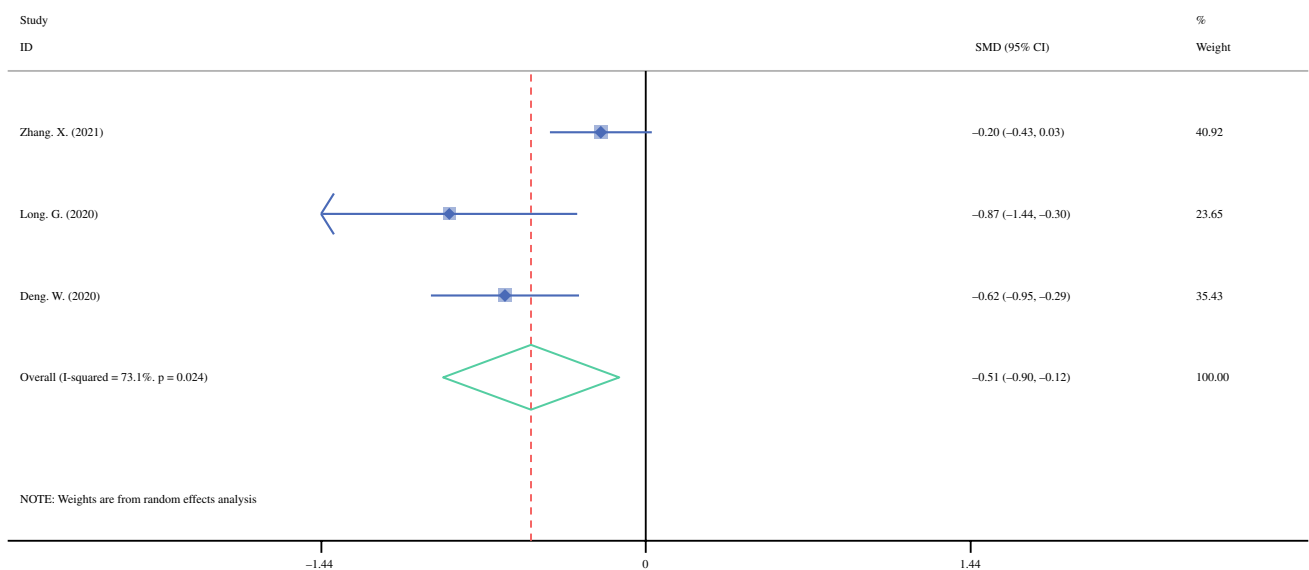


FIG. 4 Forest plot and meta-analysis of EBL between RN and PN scores

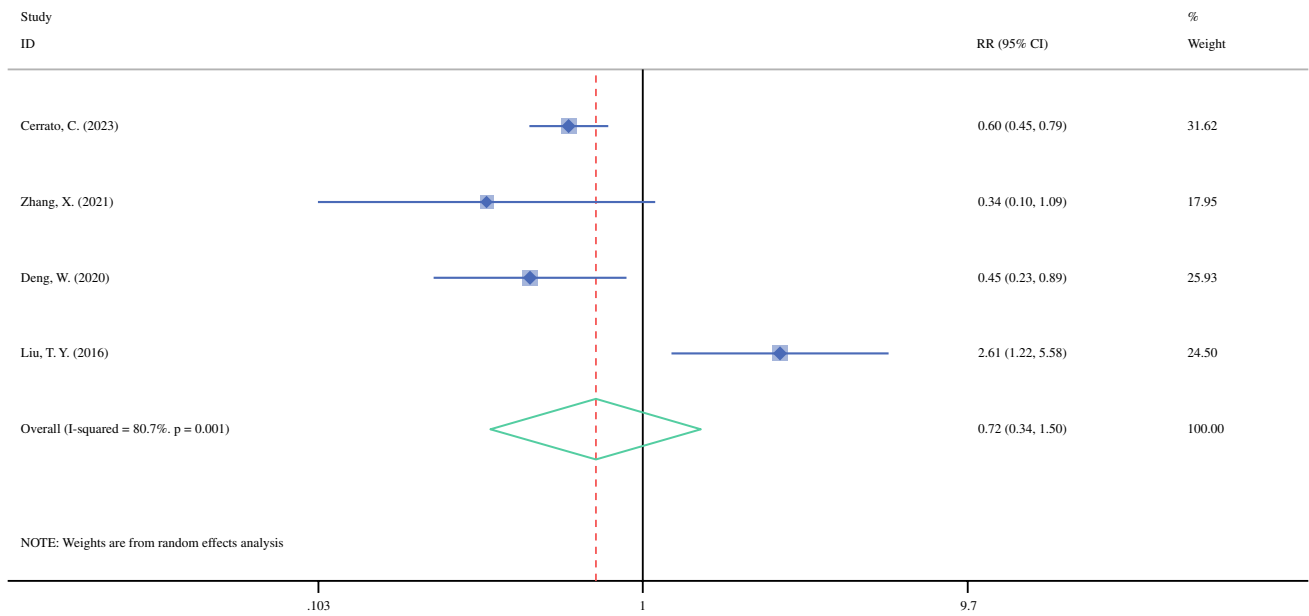


FIG. 5 Forest plot and meta-analysis of complications between RN and PN scores

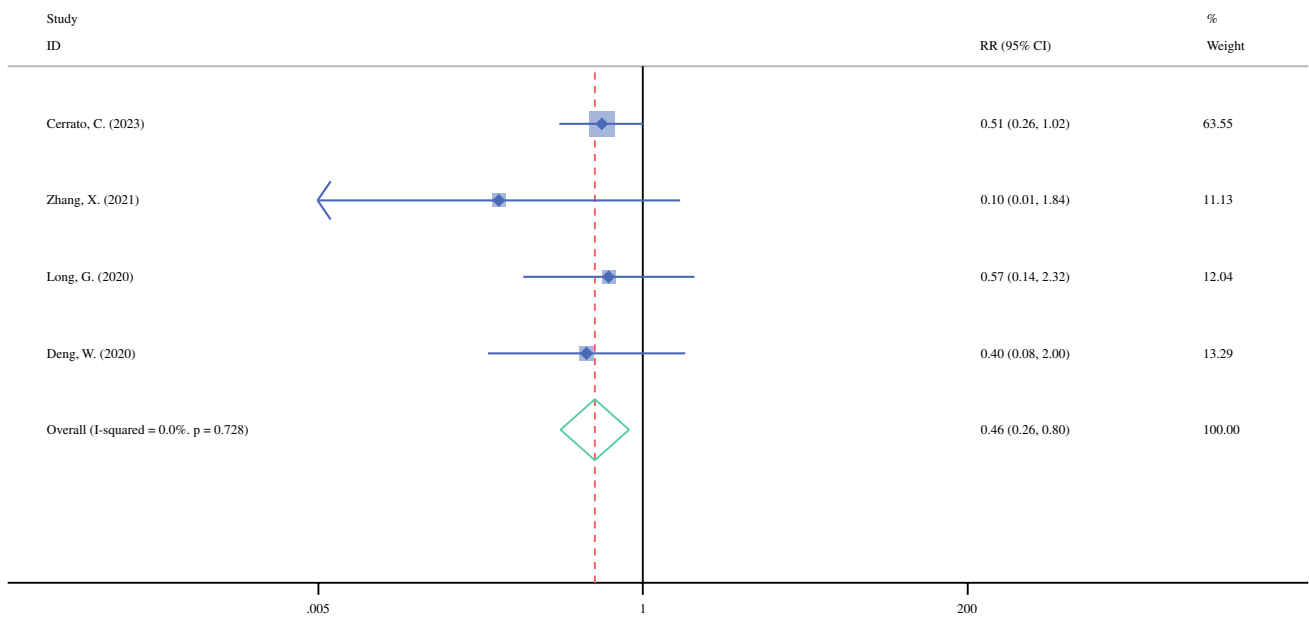


FIG. 6 Forest plot and meta-analysis of major complications between RN and PN scores

fixed-effects model. The pooled meta-analysis demonstrated no significant difference between the RN and PN (RR = 0.84, 95% CI [0.43, 1.64], $P > 0.05$) (Fig. 7).

Decreased Glomerular Filtration Rate

Three studies reported decreased glomerular filtration rate (GFR). Because of high heterogeneity ($I^2 = 77.9%$, $P = 0.024$), we used a random-effects model. The pooled

meta-analysis demonstrated significant difference between the RN and PN (SMD = 0.73, 95% CI [0.44, 1.01], $P < 0.05$; Fig. 8).

Overall Survival

Four studies reported OS. Because of low heterogeneity ($I^2 = 0.0%$, $P = 0.550$), we used a fixed-effects model. The pooled meta-analysis demonstrated significant difference

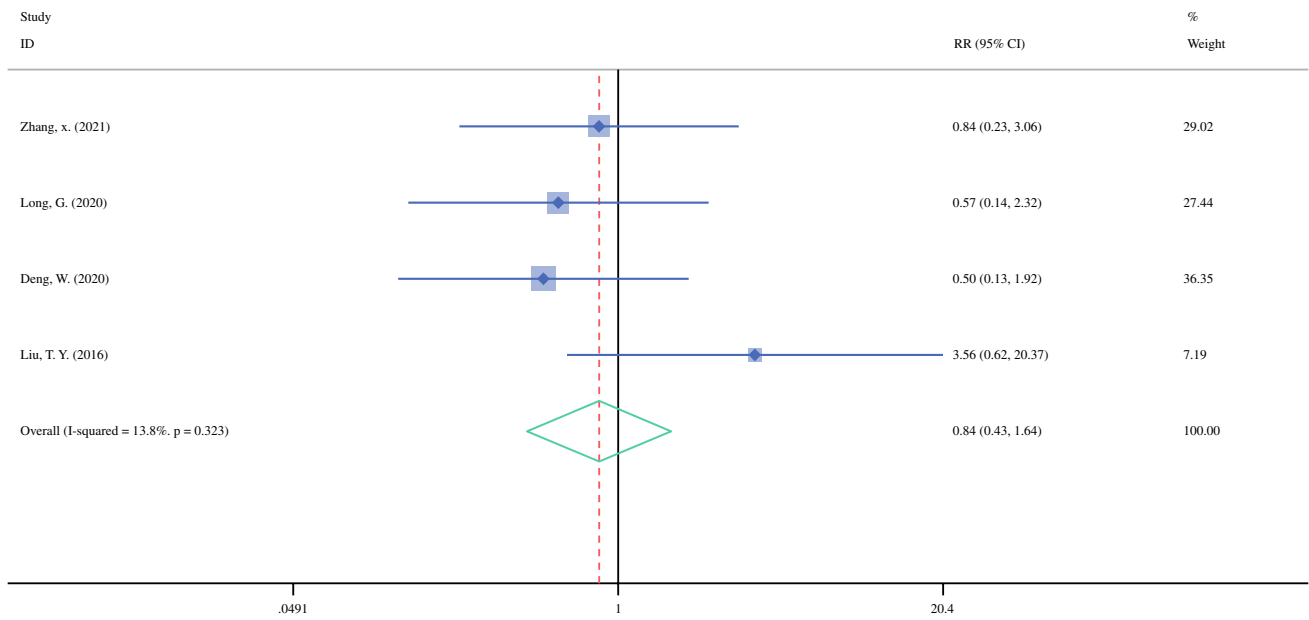


FIG. 7 Forest plot and meta-analysis of blood transfusion need between RN and PN scores

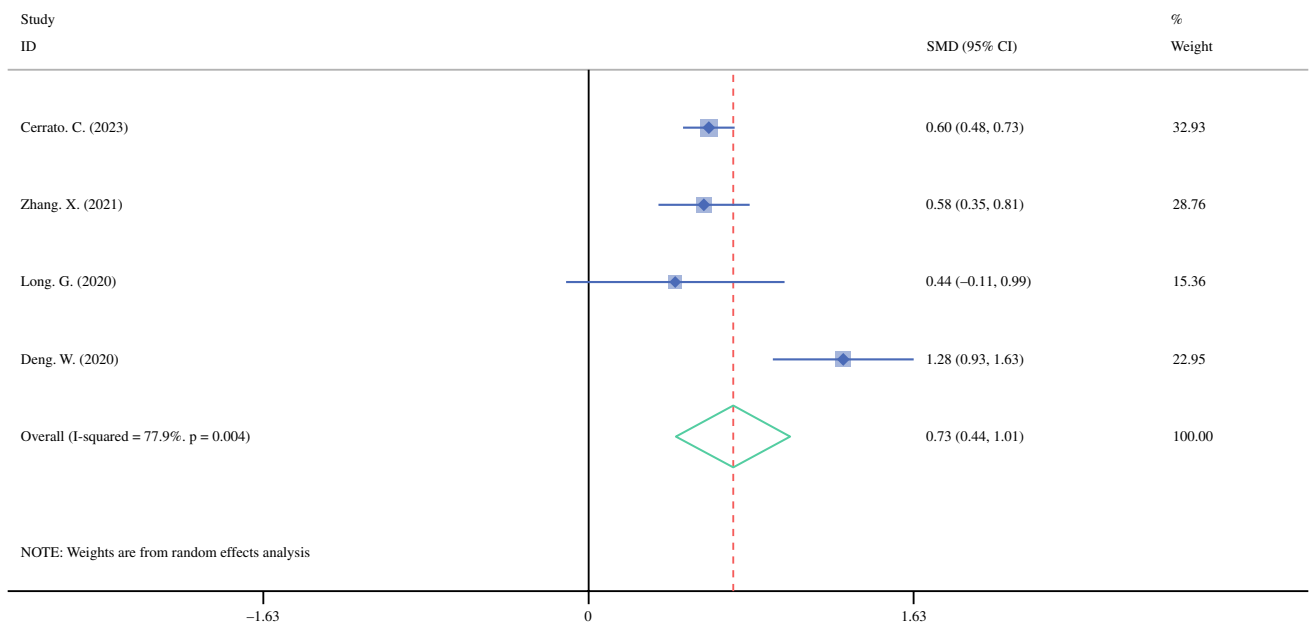


FIG. 8 Forest plot and meta-analysis of decreased GFR between RN and PN scores

between the PN and RN (HR = 1.97, 95% CI [1.38, 2.81], $P < 0.05$; Fig. 9).

Relapse-Free Survival

Two studies reported RFS. Because of high heterogeneity ($I^2 = 76.6%$, $P = 0.039$), we used a random-effects model. The pooled meta-analysis demonstrated no significant

difference between the PN and RN (HR = 1.91, 95% CI [0.72, 5.05], $P > 0.05$; Fig. 10).

Cancer-Specific Survival

Three studies reported CSS. Because of low heterogeneity ($I^2 = 0.0%$, $P = 0.392$), we used a fixed-effects model. The pooled meta-analysis demonstrated significant difference

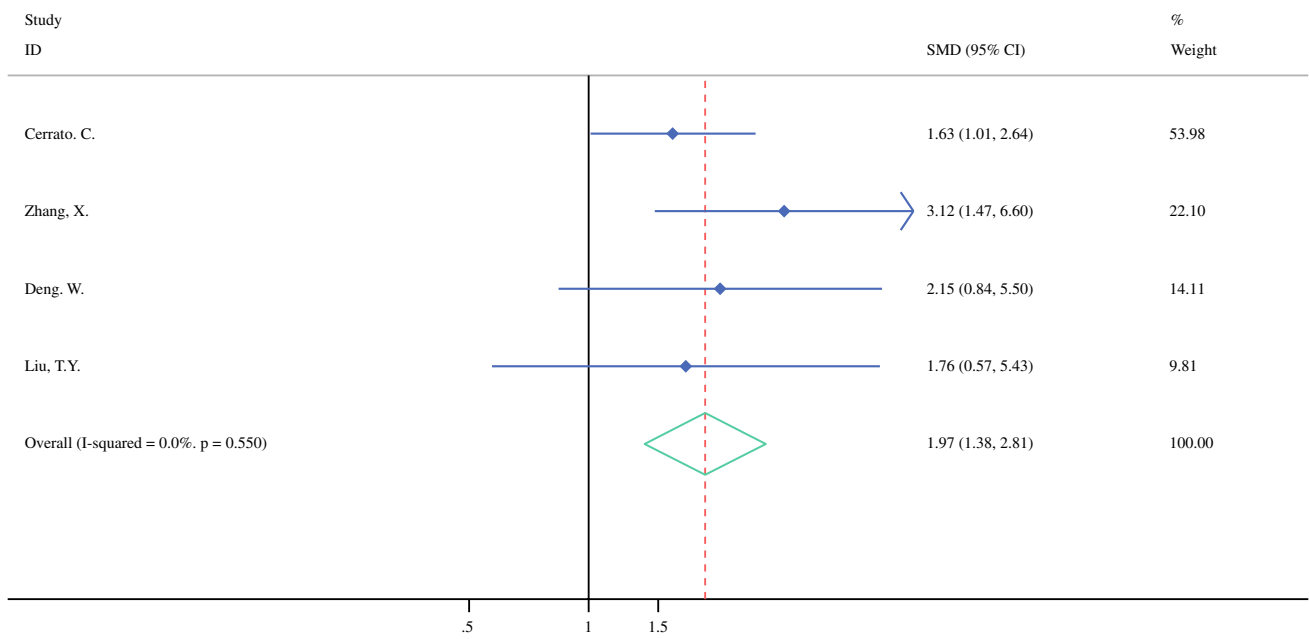


FIG. 9 Forest plot and meta-analysis of OS between PN and RN scores

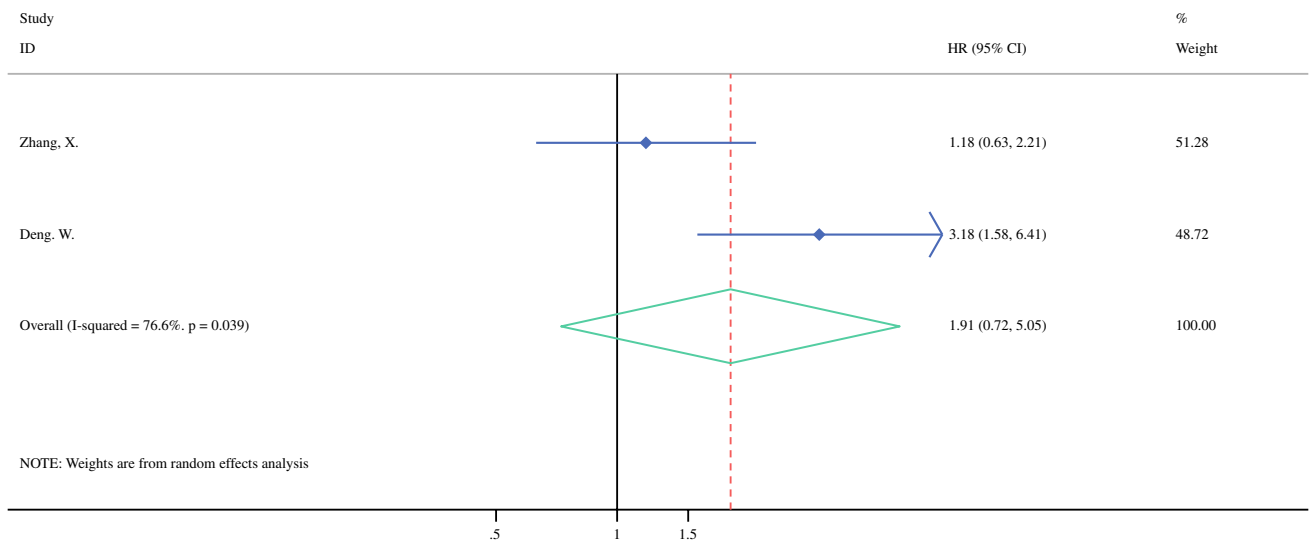


FIG. 10 Forest plot and meta-analysis of RFS between PN and RN scores

between the PN and RN (HR = 1.86, 95% CI [1.11, 3.14], $P < 0.05$; Fig. 11).

SENSITIVITY ANALYSIS

We used sensitivity analyses to track sources of heterogeneity for each outcome measure. The results showed a stable source of OT, LOS, EBL, complications, blood transfusion needs, GFR, OS, RFS, CSS, and heterogeneity.

DISCUSSION

Renal cell carcinoma (RCC) is the sixth most common cancer in men and the tenth in women, accounting for 5% and 3% of all cancer diagnoses, respectively.²² The incidence of RCC is increasing.^{22,23}

Treatment of renal tumours should ensure satisfactory perioperative, functional and oncological outcomes. Previous studies have explored different surgical approaches to PN for the treatment of complex renal tumours,^{24,25} but

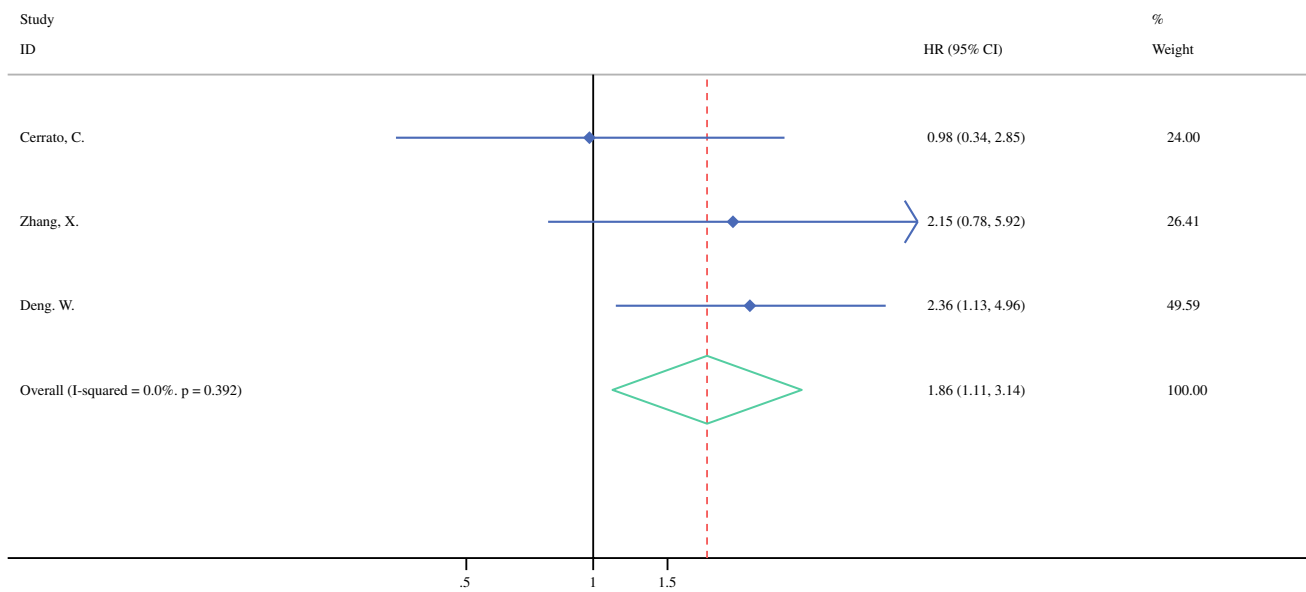


FIG. 11 Forest plot and meta-analysis of CSS between PN and RN scores

comparing PN and RN in the treatment of complex renal masses remains controversial. There were no significant differences in complications, length of hospital stay, and blood transfusion. In terms of oncological outcomes, the PN group had longer OS, CSS, and no significant difference in RFS.

Four studies reported OT. The heterogeneity test showed high heterogeneity between studies ($P < 0.10$). This difference may be due to differences in medical level and surgeon's proficiency in surgery in different regions. The pooled meta-analysis demonstrated significant difference between RN and PN. This reflects the fact that PN is a more complex procedure than RN, because it includes all the steps of RN in addition to tumour resection and renal reconstruction.

Four studies reported LOS. The heterogeneity test showed high heterogeneity between studies ($P = 0.000$). This difference may be due to differences in medical level in different regions. The pooled meta-analysis demonstrated no significant difference between RN and PN. Although PN had a higher EBL than RN, the difference between the groups was less than 100 ml and therefore unlikely to be clinically significant. This can also be supported by transfusion requirements.

Three studies reported EBL. The heterogeneity test showed high heterogeneity between studies ($P = 0.024$). The pooled meta-analysis demonstrated significant difference between the RN and PN. It is not hard to understand that more OT and more surgical steps lead to an increase in EBL.

According to the Clavien-Dindo score, there were no significant differences in complications, while there was significant difference in high-grade complications. PN is a more complex procedure than RN and the potential risks may be greater for larger and more complex masses,

thus requiring more extensive parenchymal resection and reconstruction. The reason for the difference between overall and major complications may be uncounted minor complications (Clavien-Dindo score). In Zhang et al.¹⁷ study, minor complications were, between the two groups, not significantly different.

Four studies reported blood transfusion needs. The heterogeneity test showed low heterogeneity between studies ($P = 0.323$). The pooled meta-analysis demonstrated no significant difference between the RN and PN ($P > 0.05$). PN increased EBL but did not increase the patient's blood transfusion needs.

Three studies reported decreased GFR. The heterogeneity test showed high heterogeneity between studies ($P = 0.004$). The pooled meta-analysis demonstrated significant difference between the RN and PN ($P < 0.05$). 4 studies reported OS. The heterogeneity test showed high heterogeneity between studies ($P = 0.004$). The pooled meta-analysis demonstrated significant difference between the RN and PN ($P < 0.05$). Two studies reported RFS. The heterogeneity test showed high heterogeneity between studies ($P = 0.039$). The pooled meta-analysis demonstrated no significant difference between the RN and PN ($P > 0.05$). Three studies reported CSS. The heterogeneity test showed high heterogeneity between studies ($P = 0.0392$). The pooled meta-analysis demonstrated significant difference between the RN and PN ($P < 0.05$). PN preserves renal function better than RN, leading to a lower incidence of CKD, and decreased renal function is associated with increased severe serious cardiovascular disease, OS, and CSS. This was confirmed in a study by Weight et al.²⁶

The standardized nephrometry scoring system (R.E.N.A.L. Nephrometry Score) is used to quantify the anatomical characteristics of renal masses on computerized tomography/magnetic resonance imaging.

Our research is not without limitations. First, the source of publications is limited, and we have not been able to retrieve unpublished research, so it may inevitably introduce publication bias. Second, because of the small number of studies available, we cannot predict outcomes based on different scoring stages. Third, because there are not many studies, and most of the included studies have a small sample size, the reliability of this finding needs to be further confirmed.

CONCLUSIONS

For complex renal tumours, PN requires more operative time and has a higher chance of complications in the short term. However, in long-term follow-up, PN has a small decrease in renal function with longer OS and CSS.

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